Remarks

I. Amendment to Specification to Claim Benefit of Earlier Filing Date

In accord with 37 C.F.R. §1.78(a)(2) and 35 U.S.C. §120, the application has been amended to make a claim to the benefit of co-pending U.S. Application No. 09/940,406. This claim is being made within four months of the actual filing date of the instant application, thus falling within the required time period. Also, the instant application and the earlier 09/940,406 application include at least one inventor in common, Chih-Ping Liu.

Applicants respectfully request entry of the amendment and recognition of the priority claim.

II. Pending claims

Claims 1-17 pending in the application include a single independent claim 1 and claims 2-17 dependent thereon. Independent claim 1 is directed to a method for up-regulating the blood interleukin-10 (IL-10) level in a human subject. The key elements of the claimed method are:

(i) orally administering interferon-tau (IFNτ) to the subject;

(ii) at a daily dosage of greater than 5×10^8 Units to produce an initial measurable increase in the subject's blood IL-10 level, relative to the blood IL-10 level in the subject in the absence of interferon-tau administration, and

(iii) continuing to orally administer interferon-tau to the subject on a regular basis of at least several times per week, independent of changes in the subject's blood IL-10 level, until a desired clinical endpoint is achieved.

The remaining dependent claims in the application further limit the claimed method as to

(i) the identity of the IFNτ administered (claims 2, 3);

(ii) intestinal administration (claim 4);

(iii) conditions being treated (claims 5-15); and

(iv) a further step of administering a second therapeutic agent (claims 16-17).

None of the dependent claims should be considered independent or distinct from claim 1 since they are all directed to the same subject matter (treating a condition responsive to IFN-tau) and all involve the same basic treatment steps acting through the same mechanism.

III. The Claimed Invention

The claimed method is based on the discoveries that (i) IFNτ is active when delivered orally to a human subject, (ii) doses of greater than 5×10^8 Units provide an initial rise in blood IL-10 levels, and (iii) continued administration of such an effective dose is therapeutically effective, independent of further changes in blood IL-10 levels.

A. Advantages and Features of the Invention.

The claimed method provides an improved method for treating a variety of serious medical conditions, including multiple sclerosis, viral infection such as HCV, and cancer, for which either (i) no effective treatment currently exists, (ii) current therapies are associated with serious and sometimes debilitating side effects, and/or (iii) current therapies induce drug resistance which limits the effectiveness of the resistance. In addition, where current therapies require parenteral administration, such as IV administration or drip, additional expense and patient compliance issues can arise.

These limitations are overcome, at least partially, by the present therapeutic method, by the following features of the invention:.

(i) IFNτ is administered in a convenient oral form, such as an enterically coated tablet, that targets the protein to the intestinal tract of the subject;

(ii) the side effects associated with IFNτ administration in humans are generally quite benign, particularly when compared with the relatively debilitating effects of long-term IFNα or IFNβ administration;

(iii) because side effects are minimal, long-term treatment, e.g., for multiple sclerosis, is compatible with greatly enhanced quality of life;

(iv) an effective dose of IFNτ can be determined readily by following an initial rise in patient blood Il-10 levels or, alternatively, an effective dose can be predetermined, for

a given patient, by knowledge of an IFNτ dose known to produce such rise in blood IL-10 in a patient with that particular condition;

(v) continued treatment can be carried out at therapeutic levels of IFNτ corresponding to the initial effective dose, independent of changes in blood IL-10 levels over the treatment period; and

(vi) the treatment is compatible with concomitant therapies, e.g., anti-viral therapy in the treatment of viral infection or anti-cancer therapy in the treatment of cancers.

B. Patentability Over the Prior Art

The ability to achieve the collective advantages of the claimed method, in accordance with the presently claimed method, (see Section A above) is unsuggested in the prior art for the reasons given below. Our conclusions about the scope and content of the prior art, discussed below, are made on the basis of our review of the references listed in the attached IDS Form 1449. Copies of the references listed in the current Form 1449 are enclosed herewith.

1. The prior art does not teach doses of IFNτ that up-regulate IL-10 in human subjects

References identified on the enclosed Form 1449 as Cite No. 1-5, 7-8, 10-13, 15-18, 20, 24, 25, 27-31 (copies of journal articles enclosed; full citations provided in Appendix 1 attached herewith) all disclose the use of ovine IFNτ for the treatment of a variety of conditions, including autoimmune disorders, such as multiple sclerosis, viral infections, and cancer. Although the references suggest administration of IFNτ by oral administration, among a variety of modes of administration, they do not teach oral doses of IFNτ that would be effective in humans to up-regulate IL-10.

2. There is no evidence in the prior art that an effective dose of IFNτ can be predetermined or confirmed by following changes in initial blood IL-10 levels.

None of the effective references show or suggest an increase in human blood IL-10 levels in response to IFNτ administration at the dosage levels claimed. Further, there is no suggestion in the art that an effective dose of IFNτ in humans could be

predetermined or confirmed by a measurable increase in initial increase in blood IL-10 levels.

3. There is no suggestion in the prior art to continue long-term IFNτ administration, based on a dose determined from initial blood IL-10 response, and independent of changes in blood IL-10 levels during extended treatment.

Nowhere does the prior art show or suggest that an IFNτ dose determined to be effective based on an initial increase in blood IL-10 would provide an effective dose over an extended treatment period, independent of changes in actual blood IL-10 during the treatment period, *e.g.*, in response to a reduction in viral infection or a reduction in tumor load.

4. The claimed method is not inherently taught by the prior art.

To show inherency, it is necessary to show that the prior art in question necessarily produced the newly claimed effects, and that a person skilled in the art would recognized that the newly claimed effects were necessarily achieved. (*Continental Can Co. USA, Inc. v. Monsanto Co,* 948 F. 2d. 1264, 20 USPQ2d 1746 (Fed. Cir. 1991). Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. (*In re Robertson,* 169 F. 3d 743, 49 USPQ2d 1949 (Fed Cir. 1999, quoting from *In re Oelrich*, 666 F.2d 578, 212 USPQ 323 (CCPA, 1981).

Although the prior art discloses a range of IFNτ in treatment, there is no evidence in the prior art to suggest that any specifically disclosed IFNτ dose, or that every IFNτ dose within a specified range in the prior art, would produce a measurable increase in human blood IL-10 levels, when orally administered to a human. Unless blood IL-10 levels are actually measured following IFNτ dosing, or unless oral IFNτ doses are predetermined from patients with known conditions, actual IL-10 blood level response to any given dose of IFNτ, with respect to a given condition, and when orally administered, would be a matter of conjecture, and thus not an inherent property.

Further, it cannot be argued that a person skilled in the art would know how to select an effective IFNτ dose, in accordance with the claim, because one skilled in the art would not be aware of the target goal (elevated blood IL-10 in a human).

Since the prior art does not teach or suggest all of the steps in the claimed invention, nor provide an inherent teaching of all of these steps, nor achieve all of the advantages of the invention noted above, the prior art cannot be said to anticipate or render the claimed invention obvious. Therefore, an Notice of Allowance of the claims is earnestly solicited.

Respectfully submitted,

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Judy M. Mohr
Registration No. 38,563

Correspondence Address:
Customer No.22918
Perkins Coie, LLP
P.O. Box 2168
Menlo Park, CA 94026
(650) 838-4300

Appendix 1

Citations of References Identified by Form 1449 Cite No.

Cite No. (see Form 1449)	Document Citation
1	U.S. Patent No. 5,705,363
2	U.S. Patent No. 5,906,816
3	U.S. Patent No. 5,958,402
4	U.S. Patent No. 6,036,949
5	U.S. Patent No. 6,060,450
7	US Publication No. 2002/0013452
8	U.S. Patent No. 6,372,206
10	US Publication No. 2003/0012766
11	US Publication No. 2003/0049277
12	US Publication No. 2003/0130486
13	US Publication No. 2003/0219405
15	WO 90/09806; PCT/US90/01122
16	WO 94/10313; PCT/US93/10016
17	WO 96/28183; PCT/US96/03472
18	WO 97/33607; PCT/US97/03794
20	Alexenko, A.P. *et al*, *J. Interferon Cytokine Res.*, 17:769 (1997)
24	Khan, O.A. *et al.*, *Mult. Scler.*, 4(2):63 (1998)
25	Mujtaba M.G. *et al*, *Cell Immunol.*, 186(2):94 (1998)
27	Pontzer, C.H. *et al.*, *Biochem. Biophys. Research Comm.*, 152(2):801 (1988)
28	Pontzer, C.H. *et al.*, *Cancer Research*, 51:5304 (1991)
29	Soos, J.M. *et al.*, *J. Interferon and Cytokine Research*, 15:39-45 (1995)
30	Soos, J.M. *et al. J. Neuroimmunology*, 75:43 (1997)
31	Soos, J.M. *et al.*, *J. Neuroimmunology*, 169(5):2231 (2002)